



ABOVE • NIAID's Alonda LeCounte sacrificed a kidney to benefit her stepfather. See story on p. 7.

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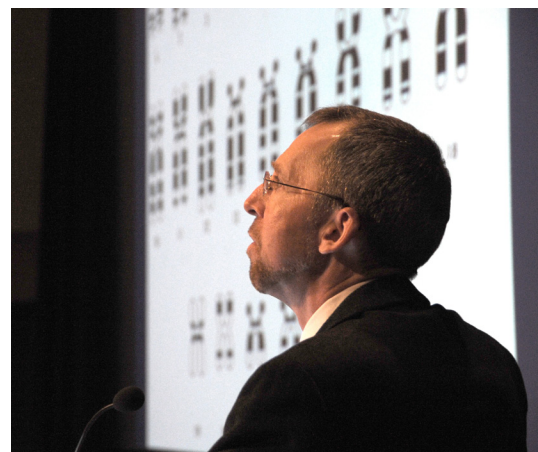
The Revolution Continues

Green Offers Tour of Genomic Landscape, Circa 2010

By Rich McManus

There is a good reason that Lipsett Amphitheater was jammed with attendees as NHGRI began its modestly titled Current Topics in Genome Analysis course—an institute staple since 1995—on Jan. 12. The 11-lecture series that ends Mar. 23 was launched by NHGRI director Dr. Eric Green, who in 90 minutes surveyed highlights of what mankind has learned of its genetic heritage starting before Mendel (1865) to the present.

A postdoctoral fellow at the outset of the Human Genome Project in 1990, Green offered a robust primer of a field that literally exploded during the “genomic revolution” of the 1990s. Having a front-row seat at what is arguably the most significant scientific endeavor of the past century gives Green both authority and a rich fund of metaphor: the 3 billion base pairs



NHGRI director Dr. Eric Green

SEE **GENOME**, PAGE 6

Anything Is Possible

MIT's Herr Works to Make Physical Disabilities a Thing Of the Past

By Valerie Lambros

NIMH's Innovation Speaker Series is intended to bring astounding people to NIH to offer lectures, but few speakers leave audiences with the feeling of awe that the institute's guest, Dr. Hugh Herr of MIT, did recently.

“Some time ago, I attended a workshop and we talked about the traits of innovative, creative people,” said Dr. David Armstrong of NIMH in his introduction of Herr. “The characteristic that stuck with me most was this ability and willingness to persist and persevere even when obstacles appear to be insurmountable. That's Hugh Herr.”

Within 30 seconds of starting his talk, Herr



SEE **HERR**, PAGE 4

Nobelist Nirenberg, Discoverer of the Genetic Code, Mourned

By Alan Schechter

Dr. Marshall Warren Nirenberg, who discovered the genetic code used by virtually all living organisms to translate the information in DNA molecules into protein structure, died of cancer Jan. 15 in New York after an illness of several months. His work is considered one of the major milestones of biological research during the last century.

“Marshall's wish to explore turned into a revelation about biology that is almost unmatched in terms of its consequences for understanding of life,” said NIH director Dr. Francis Collins. “He was not only a scientist's scientist, but a mentor's mentor...we mourn the loss of a true scientific hero.”

Nirenberg's initial contribution to solving



SEE **NIRENBERG**, PAGE 8



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briefs

Robbins To Present DDM Seminar, Feb. 18

The 2009-2010 Deputy Director for Management Seminar Series, "Management and Science: Partnering for Excellence," continues on Thursday, Feb. 18 from 11 a.m. to 12:30 p.m. in Masur Auditorium, Bldg. 10, with Dr. Steve Robbins in a presentation on "Diversity and Inclusion 2.0: A 21st Century Approach." He will discuss ways to leverage diverse perspectives for creativity, innovation and achievement of organizational goals. He is the author of *What If?: Short Stories to Spark Diversity Dialogue* and editor of *Inclusion Insights*. Videocasting and sign language will be provided. Individuals who need reasonable accommodation to attend should call (301) 496-6211 or the Federal Relay Service at 1-800-877-8339. For more information about the series, visit www.ddmseries.od.nih.gov or call (301) 496-3271.

STEP Forum on Patient Advocacy and NIH

The staff training in extramural programs (STEP) committee will present an Administrative Strategies forum on the topic "Patient Advocacy & NIH: Marriage by Choice or Necessity?" on Tuesday, Feb. 9, from 8:30 a.m. to 12:30 p.m. in Natcher conference center, Rms. E1/E2.

The role of patient advocacy groups in promoting public health issues has been controversial. Growing from social movement advocacy for faster development of AIDS treatments to current public-private partnerships, the relationship between NIH and patient advocates has come a long way. Should the practice of involving advocates in NIH activities become more commonplace? How and when should they serve as consultants for clinical research, in peer review or as program advisors to the institutes and centers? This STEP forum will discuss ways to facilitate working with advocacy groups and explore the benefits to NIH staff, scientists, advocates and, most importantly, patients.

NIH-Duke Training Program in Clinical Research

Applications are being accepted for the 2010-2011 NIH-Duke Training Program in Clinical Research. Implemented in 1998, the program is designed primarily for physicians and dentists who desire formal training in the quantitative and methodological principles of clinical research. Courses are offered at the Clinical Center via videoconference technology. Academic credit earned by participating in this program may be applied toward satisfying the degree requirement for a master of health

sciences in clinical research from Duke University School of Medicine. The degree requires 24 credits of graded course work, plus a research project for which 12 units of credit are given. The program is designed for part-time study, allowing the student to integrate the program's academic training with his or her clinical training.

Applications are available in the Office of Clinical Research Training and Medical Education, Bldg. 10, Rm. B1L403 or via email from Benita Bazemore at bbazemore@cc.nih.gov. Additional information regarding coursework and tuition costs is available via the program web site at <http://tpcr.mc.duke.edu>.

Enrollment in the program is limited. Interested individuals should inquire with their NIH institute/center regarding funding for participation. Email queries about the program may be addressed to tpcr@mc.duke.edu. The deadline for applying is Mar. 15. Successful applicants will be notified by July 1.

NCI Offers Online Course for Health Professionals

The National Cancer Institute announces the availability of Including Clinical Trials in Your Practice, a new interactive, online course for oncology professionals. This free tutorial is geared toward those who are interested in incorporating clinical trials into their oncology practices.

This new course emphasizes the importance of clinical trials, discusses challenges trial investigators face and offers solutions. It is a narrated tutorial consisting of 8 modules and includes case studies and exercises to enhance the user experience.

With this course, oncologists will understand the process and steps involved in weaving NCI-sponsored clinical trials into their practice. It can also serve as an orientation or a refresher on best practices.

To access the course, see www.cancer.gov/clinical-trials/course?cid=ctcourse_record.

Sailing Association Open House, Feb. 25

The NIH Sailing Association invites everyone to its open house on Thursday, Feb. 25 from 5 to 8 p.m. at the FAES House at the corner of Old Georgetown Rd. and Cedar Ln. Would you like to learn to sail? Can you imagine being part of a group of skilled sailing instructors, enthusiasts and boat owners? The club offers instruction, sailboats for charter, racing, cruises, parties and fun. Open house is \$5 at the door and includes pizza and sodas; cash bar for beer and wine, \$1 each. Look for NIHSA posters and flyers around campus. For more information, visit www.recgov.org/sail.

nih record



Above, NHGRI director Dr. Eric Green and NIH chief of staff Dr. Kathy Hudson (r) welcome Nobel Prize winner Dr. Carol Greider to NIH. At right, Greider, an expert on telomerase, delivers NHGRI's annual Trent Lecture.

PHOTOS: BILL BRANSON

2009 Nobel Laureate Greider Delivers Trent Lecture

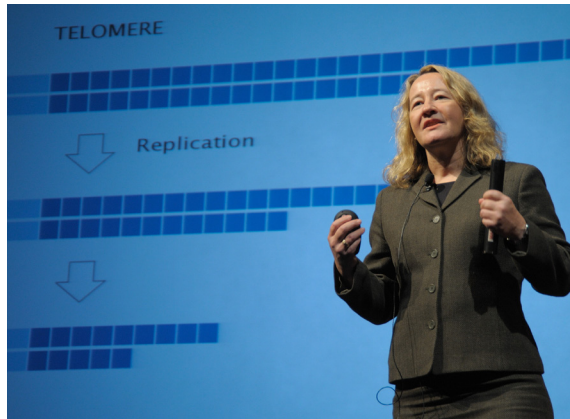
Nobel Prize winner Dr. Carol Greider presented the seventh annual Jeffrey M. Trent Lecture in Cancer Research on Jan. 19 in Masur Auditorium. A capacity audience assembled, eager to hear the lecture that had been postponed twice last year—once due to President Barack Obama's inaugural NIH visit in September and again in December when Greider traveled to Stockholm for the Nobel ceremony.

The Daniel Nathans professor and director of the department of molecular biology and medicine at Johns Hopkins Institute for Biomedical Sciences, Greider won the 2009 Nobel Prize in Physiology or Medicine “for the discovery of how chromosomes are protected by telomeres and the enzyme telomerase.” She shared the prize with Dr. Elizabeth Blackburn of the University of California at San Francisco and Dr. Jack Szostak of Harvard Medical School, Massachusetts General Hospital and the Howard Hughes Medical Institute.

Greider's lecture, “Telomerase and the Consequences of Telomere Dysfunction,” was her first public lecture since receiving the Nobel. NHGRI director Dr. Eric Green, the lecture's founder, initially invited Greider to NIH last year and it was obvious that he was excited to have her finally give the lecture.

“If you look at your program, you will note that the date of this lecture was Tuesday, Sept. 29, 2009,” said Green in opening remarks, describing how he had to reschedule the lecture. “Then Carol had to win the Nobel Prize. She explained she had to go to Sweden for the week. I understood when she called to say that we would have to postpone again.”

Green then turned the podium over to NIH chief of staff Dr. Kathy Hudson to introduce the guest speaker. Hudson and Greider have been friends for 25 years. They met while attending



I had to go to Stockholm, she said I have the best girlfriend story ever...my friend won the Nobel Prize,” Hudson said.

Greider then took the podium. “It's always good to come somewhere and talk some science,” she remarked.


She began by recounting her days as a doctoral student in Blackburn's laboratory at Berkeley. That was where she initially discovered and characterized the activity of the enzyme telomerase that maintains telomeres, from the ciliate *Tetrahymena*. Telomeres are repetitive stretches of DNA that protect and are located at the ends of chromosomes.

Greider described subsequent years, recalling how as an investigator at Cold Spring Harbor Laboratory in the early 1990s she worked with Dr. Calvin Harley to show that human telomeres shorten progressively in primary human cells. This work, combined with other telomere research being done at the time, illustrated the critical role of telomere length and its role in cell aging (senescence), cell death (apoptosis) and cancer.

In 1997, she moved her laboratory to Johns Hopkins. There, her group continued to study the biochemistry of telomerase and determined the secondary structure of the human telomerase RNA. She also expanded her work on a mouse model of the rare disorder dyskeratosis congenita and stem cell failure in response to short telomeres. Greider currently studies both the biochemistry of telomeres and telomerase as well as the cellular organismal consequences of short telomeres.

The progressive shortening of telomeres corresponds to DNA damage and age-related diseases. In addition to their association with cancer, shortened telomeres can lead to liver disease, bone marrow failure and immunologic disorders.

Greider said that she and her research team continue to work on understanding such disorders by attempting to find ways to re-establish telomere length. Her team is also studying the effect on human health of short telomere length when combined with environmental factors.

The remainder of her lecture outlined implications of telomere and telomerase research both for cancer cells, which undergo frequent replication, and for tissue-specific stem cells that may lead to therapies in the future. The lecture may be viewed online at <http://videocast.nih.gov/>. 

graduate school at the University of California, Berkeley. Hudson shared photos and humorous stories of Greider from that period. To the crowd's delight, she also had pictures of the Nobel Prize ceremony, which she attended as a guest of Greider's.

“When I told a friend at NIH that I was going to miss a meeting because

HERR

CONTINUED FROM PAGE 1



Dr. Hugh Herr, director of the biomechatronics group within MIT's Media Lab and a double amputee, says he would never consider himself disabled. He foresees a world in which disabilities are rendered obsolete with the aid of technology.

PHOTOS: ERNIE BRANSON

not only acknowledged, but seemed to welcome, the 800-pound gorilla in the room—the matter of his legs.

Standing in front of the podium and facing the audience with a quiet resolve, Herr stated plainly, “I stand before you supported entirely by artificial means.”

Wearing a pair of active prosthetics that no one would suspect were under his pant legs had he not said so, Herr said he does not see himself as disabled.

“I have a condition just as a person with eye-glasses has a condition,” he said, noting that he saw many people wearing glasses in the audience and that no one would consider labeling those people disabled. “We’re at that point because of good technology that my condition is not a disability.”

Herr is a somewhat unlikely pioneer. As an unexceptional high school student who was more focused on the outdoors than on his textbooks, he was a risk-taker who thought life was just one wilderness adventure after another. Everything changed when a 1982 mountain climbing trip took a wrong turn and he and a friend became stranded in freezing temperatures for 4 days with no shelter. Following a tragic rescue that killed a volunteer, Herr landed in the hospital. Severe frostbite eventually required that both of his legs be amputated below the knee.

What followed was a painful personal journey that transformed Herr into one of the world’s foremost scientists in the field of prosthesis and orthosis—artificial limbs and joints that give back true functionality of the limb to the wearer.

Not long after his fateful incident, Herr wanted nothing more than to get back on the horse, or mountain, as it were. So he headed into the machine shop and started crafting his first active prosthetics. By not trying to duplicate the missing portions of his legs, he found that he could craft anything his mind imagined, including artificial limbs that could let him climb higher and with greater ease than before the accident.

Fascinated by the possibilities of what technology could offer humankind, Herr’s life course was then set. After a bachelor’s degree in physics and a master’s in mechanical engineering, Herr’s Ph.D. in biophysics brought everything together for him. He now leads the biomecha-

tronics group within MIT’s Media Lab and has served on research review panels for numerous organizations, including NIH.

Herr, a soft-spoken, gentle man whose understated way of explaining the mechanics of prosthetic science impressed the Neuroscience Center audience, seemed almost unfazed by the magnitude of the research he was presenting and what it means for people with physical challenges who’ve had few choices when it comes to regaining their mobility. That is, until now.

Amputees who can walk naturally again. Stroke victims who regain their pre-stroke strides with the help of science. Technology and nature working seamlessly to erase disability. Truly, it’s mind-boggling stuff, but Herr talked about it with all the grace of a guy who’s been able to see incredible potential because he’s often his own test subject.

“It’s good to mess with people’s minds and their labels” about disability, Herr said. “We’re at a point in history where we’re going through a shift in consciousness. We’re blurring the boundaries between disabled and abled, and beyond that, augmentation.”

Herr dreams of a world in which disability is largely eliminated because of technology and people are able to achieve more with the aid of adaptable, technological helpers. This means help not only for amputees, but also for stroke and accident victims and people with cerebral palsy or muscular dystrophy for whom movement is difficult.

“I think in this century we’ll largely eliminate disability through a sophisticated machine-human interaction,” he said. “You can call them extreme interfaces.”

Think *Star Wars* or the *Six Million Dollar Man* and you’ll get the idea.

But Herr also sees applications to protect the elderly or others who may be unsteady on their feet. He said the annual cost of falls approaches that of cancer, in terms of suffering, treatment and recovery.

“We have technology now to make this table smart—that senses the fall and becomes as soft as pillows. Same for bathtubs and tile floors,” he said.

For now, Herr is focused on advancing prosthetic science ever further, examining what could make orthoses more natural, more effective, more useful. The mountains he scales these days are conceptual as he tries to realize his goals.

“We ain’t seen nothing yet,” he said. ●

Harvard's Frenk Speaks on Globalization And Health

Dr. Julio Frenk, dean of Harvard School of Public Health, recently spoke to a standing-room-only crowd in Masur Auditorium on "Globalization and Health: The Role of Knowledge in an Interdependent World." A leading authority on global health, Frenk was the guest speaker at the 2009 Barmes Global Health Lecture. NIDCR and the Fogarty International Center jointly host the annual lecture, which honors the late David Barmes, a special expert for international health at NIDCR.

"If we are to meet the challenges and reap the opportunities of an increasingly interdependent world, we need to renew global cooperation in health," Frenk said. "In this renewal process science plays an absolutely critical role." He called for international cooperation on health issues affecting people around the world and said that domestic and global health are now interconnected.

Frenk described global health issues as more complex today than ever before. Global health should no longer be thought of simply in terms of communicable diseases in developing countries, he said. Communicable diseases such as swine flu, HIV and others affect people all over the world. Chronic conditions such as heart disease and diabetes now also appear in developing nations as their populations adopt Western habits.

Because of increases in life expectancy, larger urban populations and slowed fertility rates, there has been a fundamental shift in patterns of disease, he said. That shift is toward higher age groups and toward chronic conditions, whether communicable or non-communicable.

Frenk explained that, in fact, the whole meaning of illness has been transformed. "Previously, the experience of disease was marked by a succession of acute episodes from which one either recovered or died," he said. "Now, people spend substantial parts of their lives in less than perfect health, coping with a chronic condition. Illness may not always kill us, but it always accompanies us."

Knowledge is the key for improving health around the world, he said. "Research is a value in itself, an essential part of human culture," he explained. "At the same time, knowledge has an instrumental value as a means to improve health." That knowledge, Frenk said, can be translated into new diagnostic technologies and



Shown at the Barmes Lecture are (from l) NIDCR director Dr. Lawrence Tabak, Dr. Julio Frenk, FIC director Dr. Roger Glass and NIH director Dr. Francis Collins.

new treatments and can be used by individuals as well to improve their personal health and hygiene practices.

Knowledge can also be translated into evidence that provides a scientific foundation both for specific health care services and for policy formulation, he said. He discussed his experiences as Mexico's health minister and his implementation of comprehensive national health insurance, which expanded access to health care to tens of millions of previously uninsured Mexicans. He said the reform began with scientifically derived evidence and culminated with rigorous evaluation; he described the program as "a textbook case of evidence-based policy designed and implemented making use of the best available knowledge."

Frenk said he remains optimistic about the international community's ability to face complex global health challenges and about the application of scientific knowledge for solving those challenges. "Knowledge will continue to be the key asset to sharpen our understanding of problems and to create novel solutions," he said. "In our turbulent world, still scarred all too often by intolerance and exclusion, science remains as the most powerful force for enlightened social transformation." 📖

Chef To Demonstrate *Keep the Beat* Recipe on Campus

To celebrate American Heart Month this February, the National Heart, Lung, and Blood Institute and Eurest Dining Services are partnering to support awareness and prevention of heart disease through the promotion of a new cookbook, *Keep the Beat Recipes: Deliciously Healthy Dinners*.

On Tuesday, Feb. 23, the Bldg. 10 B1 café will host a cooking demonstration of a *Keep the Beat* recipe by Culinary Institute of America-trained chef/instructor David Kamen, who created many of the recipes in the book. The café will also serve a recipe from the cookbook.

The cookbook includes 75 simple and delicious recipes with an American flair, Latino roots, Mediterranean inspiration and Asian styles. All of the recipes are based on heart-healthy principles from NHLBI, reflect the Dietary Guidelines for Americans and include a nutrition analysis.

The Eurest/NIH cafés (Bldg. 1, 10 B1 and second floor, 31, 35, Rockledge) will participate in the promotion by featuring recipes from the cookbook every Tuesday this month. The cookbooks will be sold in the Eurest cafés for \$5 during February and are also available for purchase in several R&W stores around the NIH and Rockledge campuses.



GENOME

CONTINUED FROM PAGE 1

Above:

NHGRI's Green says, "Genomics has not gotten dull since the end of the Human Genome Project. It has been a spectacular 7 years since 2003. The genomic revolution continues."

PHOTOS: MAGGIE BARTLETT

that constitute the human genome are an encyclopedia set that can be rationally broken down into volume, chapter and page. Each passing year offers scholars engaged in deciphering the Book of Life (Green cheerily counts himself among the ranks of "genome geeks") new insights into its meaning and role in health and disease.

It is somehow heartening to hear the numbing array of G's, C's, T's and A's that constitute our genomes described as "ridiculously large amounts of information," and to hear the latest generation of DNA sequencing technologies dubbed "fancy, shmancy." Anything that makes the topic seem less daunting is appreciated.

While non-genome geeks may believe that the Human Genome Project ended in October 2004 when the finished sequence was published [April 2003 was the actual project finish date], Green asserts that the project itself "is not the end of genomics, but the beginning. There are many new frontiers to be built on the Human Genome Project foundation. Now the challenge is the application of genomics to human health. How do we realize the promise of genomic medicine?"

Green noted that we don't yet have the entire genome, either. "The centromeres and other parts of chromosomes still can't be fully recovered," he said. "It is hard and expensive to completely finish a genome sequence, but it's only a very small percentage that is missing. Even now, we continue to fill in parts and learn a lot about the human genome."

Green said several major steps lie ahead for genomics. "The Human Genome Project covered

mapping and sequencing," he said. "Completely interpreting the human genome sequence may take decades. It is a huge undertaking."

Key questions include: What parts of the genome are functional, and which are not?

"About 5 percent of the human genome is evolutionarily constrained across mammalian species and presumed to be functional," said Green. "The problem is, we don't know where [the roughly 150 million functional base pairs] are."

Within that 5 percent, about 1.5 percent of the genome encodes for genes, which are thought to number around 20,000 and to be involved in production of far more than that number of proteins. Green said we have a good inventory of those gene sequences at present. But that leaves roughly 3.5 percent of the genome as non-coding functional sequence. These regions include gene regulatory elements, chromosomal functional elements and undiscovered functional elements not yet described in any textbooks.

"For example, there's a whole RNA world out there that's functionally important but not by coding for protein," he said. "We have a poor inventory of these elements, but it is a major priority in genomics now to develop one."

That knowledge gap is being addressed by another major effort—comparative sequence analyses. Green said that evolution can serve as a "consultant" to genomics by pointing to areas of the human genome that are highly conserved with other mammals.

"We know that highly conserved regions of the genome are most often functionally important, but this is not always the case," he cautioned. A major effort to "skim read" the genomes of a large set of mammals as a means to find the most-conserved parts of the human genome has recently been completed.

Another challenge is to find out what the important stretches of sequence actually do, and a project called ENCODE (Encyclopedia of DNA Elements) is doing just that across the human genome, said Green. "Richer and more detailed views of the human genome are now emerging," he said.

Green said intra-species sequence comparisons are also essential. "Which differences among us are relevant?" he asked. All humans are roughly 99.7 percent identical at the level of their DNA sequence, which leaves 3 million to 5 million base pairs differing among individuals. "Most [variants] are innocent," Green noted, "and have no phenotypic consequence, but some are metaphorical bombs."

To find variants that contribute to disease, the HapMap project and numerous efforts using genome-wide association studies (GWAS) were pursued. “The number of variants that have been found to confer risk has been exploding yearly,” Green reported. “It’s been a remarkably successful effort.”

Green said that GWAS results increasingly show that “regions conferring risk very often [perhaps 70-90 percent of the time] reflect non-coding parts of the genome...the non-coding functional landscape is of great interest in many labs now.”

The final point of Green’s talk (which is archived at www.videocast.nih.gov and would make an excellent introduction to the budding genomicist in your family, along with the course notes and syllabus available at www.genome.gov/COURSE2010/) is that DNA sequencing has become dramatically cheaper over the years. Whereas it cost upwards of \$1 billion to sequence the human genome the first time around, the goal now is to achieve the same result for \$1,000. Major progress has been made en route to that goal, Green noted.

As sequencing becomes cheaper and easier—yielding tsunamis of data—the new challenge becomes analyzing data, not generating it. “It’s like trying to get a drink of water out of a fire hose,” Green said. “It’s overwhelming, but it’s also exhilarating.”

He concluded, “Genomics has not gotten dull since the end of the Human Genome Project. It has been a spectacular 7 years since 2003. The genomic revolution continues.”

National Cancer Human Biobank Meeting

The National Cancer Institute invites you to participate in a public meeting that will announce the development of a national Cancer Human Biobank that will modernize the field of biobanking and contribute to medical advances. Come learn about the planning process and mission and review the implementation, structure, timeline and funding process.

The meeting, hosted by the Office of Biorepositories and Biospecimen Research, will take place Friday, Feb. 19 from 8:30 a.m. to noon at Natcher Auditorium. For more information call (301) 594-2212 or email biospecimens@mail.nih.gov. The session will be videocast. Visit <http://biospecimens.cancer.gov/cahub/meetings> to register for this free event.



Alonda LeCounte and Cecil Deas

NIAID Employee Donates Kidney, Gives Stepfather New Life

Over a 6-day period in December 2009, Georgetown University and Washington Hospital Center completed what is thought to be the largest kidney exchange in history. Thirteen donors each gave a kidney to 13 recipients. For Alonda LeCounte, a management analyst with NIAID’s Division of Intramural Research and one of the donors involved in this historic exchange, it was an opportunity to give a better life to someone she loved.

Her stepfather, Cecil Deas, had recently started kidney dialysis—a treatment that demands hours of being hooked up to a machine and costs up to \$80,000 a year. LeCounte asked Deas, “What do we have to do to get you off dialysis?”

LeCounte and her sister were both tested as potential kidney donors, but neither was a match. Upon receiving her test results, LeCounte was asked whether she would be willing to participate in a “living pair program,” in which she would donate a kidney to a stranger for whom she was a match, and Deas would receive a kidney from a different, matching donor.

“I didn’t give it a whole lot of thought,” says LeCounte. “I just thought it was the right thing to do.”

Over her stepfather’s protestations about the impact on her own health, LeCounte agreed to donate. Just after Thanksgiving, LeCounte received word that an exchange had been set up including her as a donor and Deas as a recipient. They underwent surgery in early December. In a matter of months, the exchange was able to accomplish what often takes years for people on the organ transplant waiting list.

LeCounte’s kidney went to Chris Conte, a 49-year-old single father of four from Frederick, Md., who was spending 10 hours a day on dialysis. He’s looking forward to folding his own clothes and putting his own socks away—a reminder of the little things so often overlooked in the daily grind. Deas received a kidney from a matching anonymous donor and has been able to stop dialysis.

“To give hope to strangers and do something good for someone you love at the same time is the greatest gift,” says LeCounte.

Media Tour Boosts Flu Vaccination Week

Dr. Anthony Fauci, director of the National Institute of Allergy and Infectious Diseases, conducted a satellite media tour during National Influenza Vaccination Week, which was Jan. 10-16. Fauci spoke to the Associated Press’s radio and broadcast channels and appeared on CNN’s *The Situation Room* to talk about how important it is for those with underlying health conditions to be protected from both the H1N1 and seasonal flu viruses by getting vaccinated. The media tour originated in NIH’s new remote video studio in Bldg. 31, a service of the Office of Communications and Public Liaison, OD.



NIRENBERG

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Nirenberg (r) was honored last November with presentation of a National Historic Chemical Landmark plaque by Dr. Thomas Lane (l), president of the American Chemical Society.

PHOTOS: BILL BRANSON

what had become a central problem in biology came in 1961, several years after he joined NIH. By the mid-1950s, largely due to the work of James Watson and the late Francis Crick, it had been realized that genetic information was contained in the chemical structure of DNA molecules and was used to determine the structure of proteins, which conduct most cellular functions. Working separately from many other investigators who were attempting more theoretical approaches, Nirenberg with his colleague Heinrich Matthaei devised an experimental approach that allowed the first demonstration of the connection between the chemical composition of DNA and that of the proteins.

Nirenberg presented his results at a small session at the International Biochemistry Congress in Moscow in the summer of 1961, but when word of his findings spread, he was asked to repeat his presentation to a large group at the congress the next day. His findings electrified the field and led to a period of great activity in the scientific community to work out the full “code” connecting the chemical sequence of the DNA nucleotides or “bases” with the sequence of the protein components, amino acids.

Working with many colleagues at NIH, Nirenberg devised several new methods and by the mid-1960s was able to develop a simple but elegant diagram—still reproduced in biochemistry and genetics textbooks—that shows the exact relationship between the four nucleotides of DNA, taken three at a time, and the 20 amino acids commonly found in proteins.

The discovery of the genetic code and the discovery of the double helix structure of DNA in 1953 are generally considered the two transformational events in making biology a molecular science and are the fundamental basis of the subsequent sequencing of the billions of nucleotides in human DNA molecules, as part of the Human Genome Project, and the sequencing of

the DNA of hundreds of other living organisms.

Nirenberg shared the 1968 Nobel Prize in Physiology or Medicine with Robert W. Holley and H. Gobind Khorana for these accomplishments and was the first NIH scientist to be so honored.

Nirenberg was born in New York on Apr. 10, 1927, but at the age of 12 moved to Orlando, where he became interested in biology. He studied at the University of Florida, where he received a B.Sc. degree in 1948 and an M.Sc. degree in 1952. In 1957, he received a Ph.D. in biological chemistry from the University of Michigan and then did 2 years of postdoctoral research at the National Institute of Arthritis and Metabolic Diseases at NIH.

In 1959, as a new research biochemist, and to the surprise of his colleagues, he began his work on the important but difficult problem of the genetic code. In 1962, he transferred to the National Heart Institute (now the National Heart, Lung, and Blood Institute) where he remained as a laboratory chief until his death. After the completion of the deciphering of the genetic code and the demonstration of its near universality in animals, plants and micro-organisms, Nirenberg’s interests turned to the application of molecular concepts and methods to the field of neurobiology. He pioneered studies of neuronal cells in tissue culture and identified signaling pathways in these cells. As recently as last year he continued to publish scientific papers on the molecular basis of memory, including the new use of genomic techniques derived from his 1960 studies “as starting points for [identifying] potentially memory-enhancing therapeutics.”

Nirenberg was among the first to call attention to potential social consequences of the new genetic techniques and was particularly appreciated by his colleagues at NIH as a mentor for young scientists and for the collaborative way in which he approached research. He was the recipient of numerous awards and honorary degrees. Last November, the American Chemical Society designated his work as a National Historic Chemical Landmark (see Dec. 11, 2009 *NIH Record*).

“Marshall’s legacy of rigorous research, intellectual curiosity and endless enthusiasm has already taken root among his colleagues at the NIH and beyond,” said NHLBI acting director Dr. Susan Shurin. “It was a pleasure and an honor to have him at the NHLBI over the past decades. He will be missed.”

Nirenberg’s first wife, the late Dr. Perola Zaltzman Nirenberg, also a biochemist at NIH, died in 2001. He is survived by his second wife, Dr. Myrna Weissman, a professor of epidemiology and psychiatry at Columbia University; a sister, Joan N. Geiger of Dallas; and four stepchildren and their children. ●

milestones

Cuthbert To Head NIMH Division

Dr. Bruce Cuthbert has been named director of NIMH's Division of Adult Translational Research and Treatment Development. A former member of NIMH's extramural program staff, he returns to NIMH following 4 years as a professor of clinical psychology at the University of Minnesota. He first came to NIMH in 1998, and was from 1999 to 2005 chief of the Adult Psychopathology and Prevention Research Branch. More recently, he had been assisting the institute since August, coordinating a project to develop neuroscience-based criteria for studying mental disorders.



Cuthbert's research is aimed at providing an understanding of how emotions, and disorders of emotional processing, originate in the interplay between the brain's most basic motivational drives. Measured differences in how individuals react to neutral and emotionally charged images—in terms of, for example, startle reflexes, heart rate, brain activity and verbal descriptions of emotional state—reveal how complex emotional responses are ultimately based in the brain wiring that implements fundamental survival-oriented drives. A model of how motivational processes relate to emotion provides a way to understand comorbidity among anxiety, mood and personality disorders and to identify risk for these disorders. Another goal is to develop diagnostic approaches that focus on symptoms that may be common to different conditions.

Cuthbert earned a Ph.D. in clinical psychology and psychophysiology from the University of Wisconsin. He served in the U.S. Army Medical Service Corps and was on the faculty at the University of Florida for 17 years. He has also held guest professorships at the University of Giessen and the University of Tübingen in Germany. He was elected president of the Society for Psychophysiological Research in 2004 and is a fellow of the Association for Psychological Science.



NCI's Ballard Retires After 39 Years at NIH

Jacquie Ballard, an NCI contracting officer with more than 39 years of federal service—35 years in procurement and acquisition—retired on Jan. 1.

Born and reared in Washington, D.C., she began working at NIH in May 1970 as a purchase order clerk. Two years later, she got a new position as a procurement clerk at NICHHD. While there, she attended Montgomery College. She also attended the University of the District of Columbia, where she received an associate's degree. In 1976, Ballard was selected as an intern in the

NIH Stride Program and accepted a position as a contract specialist at NCI. She graduated from American University in 1978, earning a bachelor's degree in contract law.

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"Jacque has supported DCP's chemopreventive agent development research group for more than 15 years as a contracting officer for our programs," said Dr. Vernon E. Steele, an acting group leader in NCI's Division of Cancer Prevention. "She has provided our group with sound contract advice and helped us in numerous ways to accomplish our mission. Jacque was very understanding of our needs and took every step to educate us in the contracting process and help us with the paperwork necessary to do our work. It is a big loss to our program to see her retire, but we know she deserves the long-awaited rest from everyday pressures. We will miss her expertise, service and helpful manner."

A life member since 1994 of Blacks In Government (BIG), Ballard is known as "Ms. BIG" among colleagues in the organization both locally and nationally. She received certification as a BIG master instructor and EEO advisor and graduated from the BIG Young Leadership Academy sponsored by the USDA Graduate School in August 2007. Ballard has served in several BIG leadership positions at every level, including regional representative, national committee chair and NIH BIG chapter president. She currently serves as one of region XI's national board members.

"Jacque Ballard's imprint on the national organization of BIG has been tremendous," notes Pentagon employee Gerald Reed, BIG region XI director and past national president. "As an elected officer at the chapter, region and national levels, Jacque has displayed leadership acumen second to none. She has continuously been sought out to provide leadership and management training at all levels of BIG."

Beyond NIH, Ballard is considered a "hand-dancing queen." She started her own dance class, Rhythm N Style, with dance partner Hawk, in May 2008. "It has been a dream come true and one of the most exciting things I've done in awhile," she noted. "In my new life of retirement, I hope to continue to meet people who love to laugh and have fun. I plan to dance until my feet have to be replaced." 🕺

Diet May Protect Against Gene Changes in Smokers

Leafy green vegetables, folate and some multivitamins could serve as protective factors against lung cancer in current and former smokers, according to a study that is a first step in understanding a complex association. The study, supported by the National Cancer Institute, appeared online Jan. 12 in *Cancer Research*. Researchers, led by Dr. Steven Belinsky of Lovelace Respiratory Research Institute, examined cells that were coughed up by current and former smokers. Upon careful study of the cells and by comparing those cells with profiles of smokers' diet, scientists found that leafy green vegetables, folate and some multivitamins could influence the prevalence of cellular gene methylation. Gene methylation, a chemical modification used by the cell to control gene expression, is likely to be a major mechanism in lung cancer development and progression as well as a potential marker for the early detection of lung cancer.

cose regulation, insulin resistance and the function of insulin-secreting beta cells in populations of European descent. Five of the newly discovered variants increase the risk of developing type 2 diabetes. The results of two studies, conducted by the Meta-Analyses of Glucose and Insulin Related Traits Consortium, provide important clues about the role of beta cells in the development of type 2 diabetes. Funded in part by NIH, the studies appeared online Jan. 17 in *Nature Genetics*. "The results give us exciting new directions for future research in the biology of type 2 diabetes, which poses a major and growing public health problem worldwide," said NIH director Dr. Francis Collins, an author of both papers.

Molecule Repairs Alcohol Metabolism Enzyme

An experimental compound repaired a defective alcohol metabolism enzyme that affects an estimated 1 billion people worldwide, according to research supported by the National Institute on Alcohol Abuse and Alcoholism. The findings, published Jan. 10 in the advance online edition of *Nature Structural and Molecular Biology*, suggest the possibility of a treatment to reduce the health problems associated with the enzyme defect. "We recently identified a molecule called Alda-1 that activates the defective enzyme, and in the current study, we determined how this activation is achieved," said study senior author Dr. Thomas Hurley of Indiana University School of Medicine. Initial investigations of Alda-1 were led by co-author Dr. Daria Mochly-Rosen of Stanford University School of Medicine.

NIDA Researchers Discover a New Mechanism Underlying Cocaine Addiction

Researchers have identified a key epigenetic mechanism in the brain that helps explain cocaine's addictiveness, according to research funded by the National Institute on Drug Abuse. The study, published in the Jan. 8 issue of *Science*, shows how cocaine affects an epigenetic process (a process capable of influencing gene expression without changing a gene's sequence) called histone methylation. These epigenetic changes in the brain's pleasure circuits, which are also the first impacted by chronic cocaine exposure, likely contribute to an acquired preference for cocaine. "Although more research will be required, these findings have identified a key new player in the molecular cascade triggered by repeated cocaine exposure, and thus a potential novel target for the development of addiction medications," said NIDA director Dr. Nora Volkow.—**compiled by Carla Garnett**



Leafy green vegetables, folate and some multivitamins could serve as protective factors against lung cancer in current and former smokers, according to an NCI-supported study.

Cancer Genome Atlas Identifies Subtypes of Deadly Brain Cancer

The most common form of malignant brain cancer in adults, glioblastoma multiforme (GBM), is not a single disease but appears to be four distinct molecular subtypes, according to a study published Jan. 19 in *Cancer Cell* by the Cancer Genome Atlas Research Network. Researchers also found that response to aggressive chemotherapy and radiation differed by subtype. Patients with one subtype treated with this strategy appeared to succumb to their disease at a rate approximately 50 percent slower than patients treated with less aggressive therapy. This effect was seen to a lesser degree in two of the subtypes and not at all in the fourth subtype. Researchers said the results may lead to more personalized approaches to treating groups of GBM patients based on their genomic alterations. The research team is a collaborative effort funded by NCI and the National Human Genome Research Institute.

Newly Identified Genes Influence Insulin, Glucose Regulation

An international research consortium has found 13 new genetic variants that influence blood glu-

NCI's Jacobson Mourned

Dr. James W. Jacobson, acting associate director of NCI's Cancer Diagnosis Program, died Dec. 23, 2009. He was 67 and succumbed to complications from leukemia.

He joined NCI in 1991 as a program director for genetics. In 1997, he became chief of what is now the Diagnostic Biomarkers and Technology Branch and continued to hold that position when he became acting head of CDP in 2008.

Jacobson made many important contributions to NCI and the cancer research community through his creative leadership in development and implementation of major translational research initiatives. Over the past year, he spearheaded NCI's national laboratory effort to characterize patient tumors at the molecular level and to validate predictive molecular assays in phase III clinical trials.

"He was a guiding light in developing the Strategic Partnering to Evaluate Cancer Signatures (SPECS) initiative, which has allowed large collaborative research groups to take comprehensive molecular analyses, define their critical components and begin incorporating them into clinical practice," said Dr. James Doroshow, director of the Division of Cancer Treatment and Diagnosis. In addition to the scientific expertise Jacobson contributed to SPECS from his seminal work on molecular signatures, particularly for lung cancer, he supplied the necessary administrative finesse to jump-start the program.

"SPECS could not be accomplished under the traditional R01 grant, and Jim was instrumental in setting up a new type of award to push the program forward," Doroshow added. "He was an incredibly generous, kind and encouraging leader who leaves a legacy of researchers who will continue his pursuits in finding reliable molecular information that will inform clinical decision-making for people with cancer."

Previous to his work on SPECS, Jacobson played a major role in the development of what is currently the Innovative Molecular Analysis Technologies Program and he developed and led the Director's Challenge initiative. Jacobson received an NIH Award of Merit for his role in the early implementation of the extramural component of the Cancer Genome Anatomy Project. Throughout his career, he convened numerous workshops to bring scientists from industry, academia and government together to discuss how to improve technology development and application for patient benefit.

Jacobson graduated from Dartmouth College, earned his doctoral degree at the University of Utah and did postdoctoral research at Yale University prior to joining the faculty of the University of Georgia. He worked for Genex Corp. for 12 years prior to joining NCI.



Have a question about some aspect of working at NIH? You can post anonymous queries at www.nih.gov/nihrecord/index.htm (click on the Feedback icon) and we'll try to provide answers.

Feedback: I am a Transhare user and like the benefit of being able to receive temporary on-campus parking permits. Recently, I found that vehicles with temporary parking permits are not allowed to park in the garage under the Natcher Bldg. I am sure the intention is not to discourage the use of Transhare, but would like to know the reason behind this decision.

Response from ORS: Employee vehicles with temporary parking permits are allowed to park in the Natcher garage and any other employee parking lot or garage on campus.

A misunderstanding with the security guard contractor has been corrected and they will cease the practice of denying entry to employees with temporary parking permits immediately.

The NIH Police and the guard contractor apologize for the inconvenience this has caused any employees in the past.

NEI Symposium Focuses on Glaucoma, Feb. 18-19

NEI is marking its 40th anniversary with a series of symposia that gather outstanding scientists who are contributing to the advancement of vision science at the bench and in the clinic.

On Feb. 18-19, the symposium "Focus on Glaucoma" is open to the scientific community within and outside NIH. Glaucoma is a severe eye disease that affects 2.2 million Americans and is the leading cause of blindness in African Americans. The talks will cover research on: control of axon growth by retinal ganglion cells and the mechanisms of neurodegeneration; genetic defects that predispose to inherited glaucoma and computational methods supporting this research; translational medicine for glaucoma and clinical trials.

On Thursday, Feb. 18, the symposium is from 2:30 to 5:30 p.m. in Lister Hill Auditorium, Bldg. 38A. On Friday, it will be held from 8:30 a.m. to 4:45 p.m. in Lipsett Amphitheater, Bldg. 10.

For an agenda, visit www.nei.nih.gov/anniversary/symposia/glaucoma.asp.



NHGRI's Dr. Joseph Ryan readies his drum kit (l) before the Rock Stars of Science rehearsal last fall. Above, Aerosmith guitarist Joe Perry follows his rhythm.

Research Fellow Ryan Attains 'Star'-ship

By Rich McManus

Please, no corny drummer jokes around Dr. Joseph Ryan, who last fall, on account of his status as both a scientist and a musician, was invited to sit in with NIH director Dr. Francis Collins and his fellow Rock Stars of Science at an event later videocast at the U.S. Capitol Visitor Center.

Rock drummers are traditionally mocked as having more brawn than brains, but that stereotype fails with Ryan, a research fellow in NHGRI's Genome Technology Branch. An evolutionary genomicist, he works within GTB's computational genomics group.

Ryan has done two stints at NIH. He began as a programmer in fall 1996 and worked for 5 years before attending graduate school. He returned to NHGRI as a postdoctoral fellow in 2006.

A convivial, music-loving institute, NHGRI holds annual picnics and retreats at which employees play home-grown music. Collins, who directed NHGRI for 15 years beginning in 1993, often played in and led bands at these events. Ryan followed his older brother Sean's steps as a drummer at NHGRI functions, and word got around that he, too, could play.

Last fall, Collins emailed Ryan with an invitation to play drums at a charity event featuring Joe Perry, the lead guitarist for the rock group

Aerosmith. The band included Perry and his bass player David Hull, Collins, Ryan and Harvard scientist Dr. Rudy Tanzi.

"It was pretty incredible playing with those guys," Ryan said. "You can really feel it when you're playing with pros."

The band practiced a handful of tunes five times each as a video crew captured the best performances for the Rock Stars of Science Briefing and Tribute sponsored in part by Geoffrey Beene Gives Back on Sept. 24.

"It went off pretty straight," Ryan remembers. "I was pretty nervous—I didn't know what to expect. I'm not primarily a drummer these days," he added, noting that his main instrument is guitar, which he plays in a group called Impossible Hair. That band is currently working on its second CD and has already toured Europe, in addition to playing gigs in the Philadelphia-Baltimore-Washington corridor.

"I could just imagine being ripped by Perry or his bassist," Ryan recalls, "but Joe Perry came in and did his thing. He was not critical at all. And his bass player was very encouraging."

Ryan did not take up music until 1998, when he was in his late 20's, and is largely self-taught. "All my friends play music," he said. Drums were his first instrument, but he has also learned guitar, bass, writes songs—most of Impossible Hair's music is original—and enjoys singing. He is also teaching himself piano.

"If I had the time, I would love to play in four bands," he said. "I'd play some kind of weird keyboards in one group, bass in another, guitar in another and sing in the fourth."

As much as he enjoys making music, Ryan has no interest in switching careers. "Music is way harder than science," he said. "Touring is very hard (as his band knows from playing 20 European cities in 3 weeks last year). And it's easier to measure success in science. Musical talent is not often rewarded. I like doing it as a hobby more."

Ryan enjoys reaching specific goals in music: release a CD, conduct a tour. "But I don't want to be dependent on external stuff," he said.

Ryan was intrigued by comments guitarist Perry gave to an interviewer at the Rock Stars of Science event. "He said he'd always wanted to be a marine biologist, and he really admired the life of Jacques Cousteau." Ryan notes that Led Zeppelin guitarist Jimmy Page, too, when interviewed as a youngster, expressed interest in a career in biology and cancer research.

"Science and music are kind of joined," Ryan said, "and most people don't realize it either."

Ryan divulged that he would enjoy sitting in with The Directors, NIH's pre-eminent erstwhile rock band, which has long featured Collins as a guitarist and singer.

"I would love to play with The Directors," he said, "but I like being a fill-in guy, too." 🎸



PHOTOS: JOHN BURKLOW, RICH MCMANUS